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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/658,621	09/08/2000	Joyce Taylor-Papadimitriou	029395-17	3359

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	23

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/658,621	TAYLOR-PAPADIMITRIOU ET AL.	
	Examin r	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 35-37* is/are pending in the application.

4a) Of the above claim(s) *4 –16 , 19 and 23-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,17,18,20-22 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09/08/00* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *22* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The **examiner** of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michail Belyavskyi, Group Art Unit 1644, Technology Center 1600

Claims 1-33 and 35-37 are pending.

2. Applicant's election with traverse of Group 25, claims 1-3, 17, 18 20-22 and 37 as they read on SEQ ID NO:26 in Paper No. 21 is acknowledged. Applicant traverses the Restriction Requirement on the grounds that the search of all Groups 1-34 together would not constitute a serious search burden on the examiner.

This is not found persuasive because the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". Moreover, for the elected group drawn to a polypeptide amino acid, the Applicant must further elect a single amino acid sequence (See MPEP 803.04). In view of limited office resources , only a single amino acid sequence will be examined in this application. In addition, to the specific selected sequence, those sequences which are patentably indistinct from the selected sequences will be also examined.

Examination will be restricted to only the elected sequences.

The Restriction Requirement enunciated in the previous Office Action meets this criteria and therefore establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in paragraphs 3-4 of the previous Office Action

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 3 ((a – e) and (g)), 4 –16 , 19 and 23-36 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-2, 3 (f), 17, 18, 20-22 and 37 read on SEQ ID NO:26 are under consideration in the instant application.

4. The first sentence of the specification should refer to the provisional application using language such as: " This application claims the benefit of U.S. Provisional Application No. 60/187,215 , filed on 03/03/2000". See MPEP 1302.04

5. Applicant's amendment, filed 4/11/03 (Paper No. 22), notes that an IDS was submitted . However the citations A1 to A-12 have been crossed out as said references cannot be found. Applicant is invited to resubmit such references to complete the instant file. The examiner apologizes for any inconvenience to applicant for having to resubmit such documents.

6. Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

7. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 29, second paragraph. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 17, 18, 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 17 is indefinite and ambiguous in the recitation of " a vector comprising said polypeptide". It is unclear how can a vector comprises a polypeptide?. Vectors typically comprises a polynucleotide encoding a polypeptide.

B. Claim 21 is indefinite and ambiguous in the recitation of " a vaccine comprising a polypeptide of , ". It is unclear what applicant means by this phrase?

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 17, 18, 20-22 and 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of SEQ ID NOs: 3 to 33 and 65 and 66 , does not reasonably provide enablement for a: (i) any polypeptide comprising at least one amino acid sequence of at most 20 consecutive amino acid defined in SEQ ID NO: 1, as recited in claim 1; or (ii) any polypeptide comprising SEQ ID NOs: 3 to 33 and 65 and 66 , as recited in claim 2 or 3; or (iii) any composition, or any diagnostical composition or any vaccine or any kit comprising any polypeptide of claim 1, as recited in claims 17, 20, 21 and 37 accordingly ; or (iv) any vaccine comprising an analogue of any polypeptide of claim 1, as recited in claim 21. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

(A) The claims as written encompass the genus polypeptide amino acid sequences. The genus encompasses peptides wherein such peptides have numerous differences in amino acid sequences.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Applicant discloses a polypeptide comprising SEQ ID NO: 1 (495 residues) and a polypeptide consisting of amino acid residues of SEQ ID NOs: 3 to 33 and 65 and 66 in the instant specification , wherein said polypeptide binding at least one MHC-I glycoprotein.(see page 7 in particular). Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies "any analogs" other than polypeptide consisting of amino acid residues of SEQ ID NOs: 3 to 33 and 65 and 66 that are capable of binding at least one MHC-I glycoprotein. Applicant has not taught how many polypeptides are included in "of at most 20 contiguous amino acid sequence of SEQ ID NO:1. Applicant has not taught how to make and/or use: (i) any polypeptide comprising at least one amino acid sequence of at most 20 consecutive amino acid defined in SEQ ID NO: 1, as recited in claim 1; or (ii) any polypeptide comprising SEQ ID NOs: 3 to 33 and 65 and 66 , as recited in claim 2 or 3; or (iii) any composition, or any diagnostical

composition or any vaccine or any kit comprising any polypeptide of claim 1, as recited in claims 17, 20, 21 and 37 accordingly or (iv) any vaccine comprising an analogue of any polypeptide of claim 1, as recited in claim 21. The structural and functional characteristics of said polypeptides and analogue are not defined in the claim.

"Comprising" is considered open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, a peptide "comprising" at least one amino acid sequence of at most 20 consecutive amino acid defined in SEQ ID NO: 1 as recited in claim 1, or (ii) any polypeptide comprising SEQ ID NOs: 3 to 33 and 65 and 66 , as recited in claim 2 or 3; or (iii) any composition, or any diagnostical composition or any vaccine or any kit comprising any polypeptide of claim 1, as recited in claims 17, 20, 21 and 37 accordingly; or (iv) any vaccine comprising an analogue of any polypeptide of claim 1, as recited in claim 21 includes an unlimited number of amino acid sequences "comprising" an unlimited number of polypeptides and analogue. The disclosure of SEQ ID NOS: 2, 3 to 33 and 65 and 66 cannot support the entire genus of any polypeptide comprising at least one amino acid sequence of at most 20 consecutive amino acid defined in SEQ ID NO: 1, as recited in claim 1; or (ii) any polypeptide comprising SEQ ID NOs: 3 to 33 and 65 and 66 , as recited in claim 2; or (iii) any vaccine comprising an analogue of any polypeptide of claim 1, as recited in claim 21, as part of their sequence that are capable to bind at least one MHC-I glycoprotein. A myriad of peptides is encompassed by the claims.

For instance, the length of the peptide is important for binding to MHC-I glycoprotein, HLA (along with the presence of anchor (or "motif") amino acid residues present within the peptide). The peptides that bind to class I molecules have a predominant length. A primary factor for this is that amino acid residues at the amino- and carboxy-termini of peptides binding to class I molecules interact with conserved amino acid residues in pockets ("A","F") located at opposite ends of the binding groove of the class I molecule, giving rise to a common orientation of the peptides in the binding site (Engelhard, Curr Opin Immunol. 6(1):13-23, 1994, at page 14, column 1, lines 16-27.) Thus, the amino acid residues at the peptides' termini make a network of hydrogen bonds with conserved residues on the sides and bottom of the peptide binding groove of class I molecules. These interactions are important for holding the peptides in the binding groove and for stabilizing the complex (Guo, et al, Nature. 360(6402):364-366, 1992, at page 366, column 1 lines 1-10.) "...the preferred length (of the peptide) is determined by the minimum amount of peptide required to span the center of the binding site and optimize the interactions at the ends." (Engelhard at page 14, column 1, lines 23-27.) The minimum amount of peptide required to span the binding groove and make favorable contacts with their N-and C-termini may be dependent upon the sequence of the peptide itself since different amino acid residues have different physicochemical properties, and may be dependent upon the identity of the additional amino acids, since these residues may make a negative contribution to binding. Accordingly, there is a high level of unpredictability in designing/selecting longer sequences that would still maintain binding function, and applicant does not provide direction or guidance to do so. Moreover, Applicant himself acknowledge that it is not possible to predict which protein will enter the antigen processing pathway, which fragments will be produced, or which fragment

will bind to MHC-I glycoprotein. Additionally it is not possible to predict which fragments T cell will recognize and whether the T cell which recognize the fragment will be protective (see page 2, third paragraph in particular).

Protein chemistry is probably one of the most unpredictable areas of biotechnology . It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular). Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (Mol Cell Biol. 8:1247-1252, 1988) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the polypeptide or an analogue thereof to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p 1306, col. 2).

Applicant is relying upon certain biological activities and the disclosure of a limited number of species does not provide the enablement to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated any peptide "comprising" at least one amino acid sequence of at most 20 consecutive amino acid defined in SEQ ID NO: 1 as recited in claim 1, or (ii) any polypeptide comprising SEQ ID NOs: 3 to 33 and 65 and 66 , as recited in claim 2 or 3; or (iii) any composition, or any diagnostical composition or any vaccine or any kit comprising any polypeptide of claim 1, as recited in claims 17, 20, 21 and 37 accordingly; or (iv) any vaccine comprising an analogue of any polypeptide of claim 1, as recited in claim 21 encompassed by the claimed invention other than "a polypeptide comprising SEQ ID NO: 1 (495 residues) and a polypeptide consisting of amino acid residues of SEQ ID NOs: 3 to 33 and 65 and 66" would be expected to have greater differences in their activities.

Since the amino acid sequence of a polypeptide determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. generation of antibodies which recognize p33) requires a knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which a polypeptide's structure relates to it's functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain functional aspects the peptides and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routing experimentation.

Since the amino acid sequence of a polypeptide determined its structural and functional properties, predictability of which fragments will retain functionality requires knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence contribute to its structure, and therefore, function. The problem of predicting which fragments or derivatives of a protein will retain functionality and which will not is complex and well outside the realm of routine experimentation. Because of the lack of sufficient guidance and predictability in determining which structures would lead to functional proteins or peptides with the desired properties and that the relationship between the sequence of a peptide and it's tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al, in The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encompassed by the claimed invention. Without sufficient guidance, the changes which can be made in the structure of "any polypeptide of claim 1 or any analogue thereof " and still specifically binding at least one MHC-I glycoprotein is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Also, at issue is whether or not the claimed composition would function as vaccine. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use vaccine as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed vaccine is effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed vaccine with a reasonable expectation of success.

By definition, a vaccine is a composition to induce a specific immunity that **prevent** or protect against a specific disease caused by a specific agent. One of the criteria for a vaccine is the levels of antibody (humoral immune response) before and after immunization and the success of vaccination is judged by the extent of increase in the level of antigen - specific antibody. The second criterion for a vaccine is the ability to stimulate memory T lymphocytes (cell-mediated immune response) (See Immunobiology, Third Edition, Chapter 13 in particular). The specification provides no information on the immunogenicity of *any* vaccine comprising *a* polypeptide as recited in claim 21 or the ability of such vaccine to protect or prevent from antigen-specific disease. The specification fails to teach that the vaccine comprising *a* polypeptide as recited in claim 21 are capable of generating an antibody response. The specification also fails to teach that the antibody response to the claimed *a* polypeptide as recited in claim 21, alone or in combination with adjuvants or carriers provides for a protection against infection. Vaccines by definition trigger an immunoprotective response in the host vaccinated and mere antigenic response is insufficient. It is well recognized in the vaccine art, that it is unclear whether an antigen(s) derived from a pathogen will elicit protective immunity. Ellis, R.W. (Chapter 29 of "VACCINES" [Plotkin, S.A. et al. (eds) published by W. B. Saunders company (Philadelphia) in 1988, especially page 571, 2nd full paragraph] exemplifies this problem in the recitation that "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.... and thus protect the host against attack by the pathogen". Moreover, Chandrasheker et al., (US Patent 6,248,329) teach that although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessary correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from specific disease, associated with said antigen (see column 1, lines 35-45 in particular). In addition, Spitler , (Cancer Biotherapy, 1995, v.10 pages 1-3 teaches that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company, and you're likely to get the same response" (see page 1, column 1, paragraph 1 in particular). The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. Ezzell (NIH Research, 1995, Vol.7, pages 46-49) reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see entire document, particularly the last paragraph). It is well known in the art that tumor cells in vivo simply do not display their unique antigens in ways that are easily recognized by cytotoxic T lymphocytes (Ezzell; page 48, column 2, paragraph 2). Furthermore, no one is very optimistic that a single peptide or a virus carrying the gene encoding that peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (Ezzell; page 48, paragraph 6).

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to make and/or use claimed: (i) any polypeptide comprising at least one amino acid sequence of at most 20 consecutive amino acid defined in SEQ ID NO: 1, as recited in claim 1; or (ii) any polypeptide comprising SEQ ID NOs: 3 to 33 and 65 and 66 , as recited in claim 2 or 3; or (iii) any composition, or any diagnostical composition or any vaccine or any kit comprising any polypeptide of claim 1, as recited in claims 17, 20, 21 and 37 accordingly; or (iv) any vaccine comprising an analogue of any polypeptide of claim 1, as recited in claim 21 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11 . Claims 1-3, 17-18, 20-22 and 37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : a polypeptide consisting of SEQ ID NOs: 3 to 33 and 65 and 66.

Applicant is not in possession of : (i) any polypeptide comprising at least one amino acid sequence of at most 20 consecutive amino acid defined in SEQ ID NO: 1, as recited in claim 1; or (ii) any polypeptide comprising SEQ ID NOs: 3 to 33 and 65 and 66 , as recited in claim 2 or 3; or (iii) any composition, or any diagnostical composition or any vaccine or any kit comprising any polypeptide of claim 1, as recited in claims 17, 20, 21 and 37 accordingly or (iv) any vaccine comprising an analogue of any polypeptide of claim 1, as recited in claim 21 .

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 17, 18, 20-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Van Baalen, C et al (WO. 98/17309), as evidenced by Rammensee et al. (Immunogenetics. 1995, 41, 178-228).

WO '309 teaches a 9 mer polypeptide of SEQ ID NO: 19 that comprises 3 consecutive amino acids of SEQ ID NO:1 of the instant application and that is 55.6 % identical to SEQ ID NO:26 of the instant application. (see entire document and sequence alignment). WO '309 teaches a composition comprising said polypeptide , a vaccine comprising said polypeptide and an adjuvant which stimulates MHC class I response (see pages 5, second paragraph; page11, second and third paragraph , page 13, third paragraph in particular).

The recitation that "said polypeptide binding at least one MHC I glycoproptein", as claimed in claim 1 is considered an inherent property of the reference polypeptide as evidence by

Rammensee et al . Rammensee et al . teach a polypeptide motif that is essential for the said polypeptide to bind with MHC-I glycoprotein , (see entire document, table 2, page 192 in particular). Rammensee et al . teach that for 9 mers for example such anchor motif (2 in most cases) should contain amino acid 'S" at position 2 and amino acid "Y" at position 9. It is noted that the referenced 9 mer polypeptide contained "S" at position 2 and "Y" at position "9" (see sequence alignment). Since the office does not have a laboratory to test the reference polypeptide, it is applicant's burden to show that the reference polypeptide do not bind to at least one MHC-I glycoprotein as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claim 18 and 20 are included because the claimed functional limitation would be inherent properties of the referenced composition, because said composition would comprises the same polypeptide as claimed . If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. an essentially pure composition of one or more members of the FRIL family) and the use is directed to a result or property of that composition or structure then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999). Further a composition is a composition irrespective of what its intended use. The term "pharmaceutical composition" or "diagnostical composition" carries little patentable weight in the absence of evidence of structural difference

The reference teaching anticipates the claimed invention.

14. Claims 1-3, 17, 18, 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Wrescshner (WO 9603502-A2) as evidenced by Rammensee et al. (Immunogenetics. 1995, 41, 178-228).

WO '502 teach a mucin-derived polypeptides and composition and vaccines comprising said polypeptides for the diagnosis, imaging and therapy of human cancer polypeptide (see entire document, Abstract in particular). WO '502 teach a polypeptide of SEQ ID NO 17, that is 100 % identical to the claimed SEQ ID NO:26 (see sequence alignment in particular). WO '502 teach a functional derivative of mucin-derived proteins of various length (see page 5 in particular). WO '502 teach a pharmaceutical composition comprising said polypeptide (see page 12 in particular.) WO '502 teach a cell culture transformed with a vector, comprising a polynucleotide encoding said proteins (see page 20 in particular). WO '502 teach a vaccine comprising said polypeptide and adjuvant which stimulate a MHC class I response. (see pages 45 –47 in particular).

The recitation that "said polypeptide binding at least one MHC I glycoproptein", as claimed in claim 1 is considered an inherent property of the reference polypeptide as evidence by Rammensee et al . Rammensee et al . teach a polypeptide motif that is essential for the said polypeptide to bind with MHC-I glycoprotein , (see entire document, table 2, page 192 in particular). Rammensee et al . teach that for 9 mers for example such anchor motif (2 in most cases) should contain amino acid 'S" at position 2 and amino acid "Y" at position 9.
It is noted that the referenced polypeptide contained "S" at position 2 and "Y" at position "9" (see sequence alignment). Since the office does not have a laboratory to test the reference polypeptide, it is applicant's burden to show that the reference polypeptide do not bind to at least one MHC-I glycoprotein as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 37 is rejected under 35 U.S.C. 103(a) as being obvious over Wrescshner (WO 9603502-A2) or over Van Baalen, C et al (WO. 98/17309) both in view of Zuk et al. (U.S. Patent No. 4,281,061)

The teaching of Wrescshner (WO 9603502-A2) and Van Baalen, C et al (WO. 98/17309) have been discussed, supra.

Wrescshner (WO 9603502-A2) and Van Baalen, C et al (WO. 98/17309) does not teach a kit comprising a polypeptide and adjuvant.

US Paten '061 teaches that reagents of the pharmaceutical compositions can be provided as kits as a matter of convenience , optimization and economy of the users (see col 22, line 62 - col 23, line 4 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Paten '061 to those of WO '502 or WO '309 to obtain a claimed kit comprising a polypeptide adjuvant.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because assemble the reagents in a kit format a matter of convenience , optimization and economy of the users as taught by US Paten '061 and the components of the pharmaceutical compositions taught by WO '502 or WO '309 can be in a pack or a kit for convenience and economy.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. No claim is allowed.

18. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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